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This is the first occasion at which I have been invited to attend a meeting of this kind. It is also a twenty-fourth anniversary of another occasion when I was a young medical student attending my first scientific conference. This was an international meeting at Cold Spring Harbor, near New York, and it could be truly labelled as the birthdate of a new scientific field, the genetics of bacteria and of viruses. My first published work was presented at that meeting and it concerned the discovery, contrary to decades of previous supposition to the contrary, that bacteria were indeed possessed of a mechanism like sexual reproduction which made it possible to crossbreed different bacterial strains. These observations, together with related ones by many other colleagues have gone into the emergence of the most powerful of new methods and insights in experimental biology, going generally under the name of molecular biology.

From the very beginning it was inescapable to me that these new approaches for the understanding and manipulation of living organisms had potential implications for human progress of very great significance. On the one hand molecular biology could increase man's knowledge about himself and lead to revolutionary changes in medicine in such fields as cancer, aging, congenital disease, and virus infections. It might also play a vital role in industry and in agriculture. On the other side it might be exploited for military purposes and eventuate in a biological weapons race whose aim could well become the most efficient means for removing man from the planet. As a student of evolution, and having studied it in the microcosmos with bacterial cultures, I knew that man had no guaranteed place on our earth. He has faced and continues to face natural disasters like the infestations that have wiped out the American chestnut and the European grapevine. To these long-standing threats would now be added new ones, potentially of our own invention.

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These past twenty-five years, in the course of which the world community has reached a certain degree of familiarity with the problems of nuclear power, and has undertaken some of the steps needed to contain it as a servant for rather than against human aims, have seen a sustained, remarkable development of molecular biology. For example, Professor Gobind Khorana recently reported the synthetic assembly of a small gene through chemical operations on DNA components. It will be a step of another order of magnitude to extend this technical capability to the synthesis of small viruses, but this surely will be accomplished within the next decade. This procedure will allow an unlimited range of experimental variations of the genetic structure of different viruses, a process which has many important potential applications for human health. It also offers us the prospect of engineering the design of viruses to exquisite detail. Accomplishments like Khorana's have been possible in a small laboratory on an annual research budget which is miniscule compared to weapons hardware. A serious military investment in this area could be expected to outstrip this already breathtaking pace of advance by many fold.

I could mention many other intriguing scientific advances from my own work and that of others, and fear only that my enthusiasm in discussing these details might outrun your patience in hearing about them. I will be glad to engage later in informal discussions on any aspect of molecular biology that may be of interest to you. I will just mention the discoveries of three methods of modifying the genetic structure of microbes: (1) cross-breeding them through what is, essentially, sexual reproduction; (2) inserting new genes carried by a virus, a process called "transduction", and (3) direct manipulation of DNA as a chemical substance, and reintroducing this into microbial cells.

I deeply appreciate the gravity and importance of the work of this Committee. Its principal significance is, of course, for the security of all the people of the world; and to that it is only a small addition to mention my own moral pre-occupation with whether my own career will have been labelled a blessing or a curse to the humanity from which I spring. This comment may have more force if I offer it as not only a personal testimony but as typical of the dilemma that faces my entire generation of biological research scientists and our younger students at this very moment. I am therefore many times indebted to you not only for your present labours but also for having offered me the privilege of a more personal participation in a process that may yet result in "civilizing" this branch of science.

For many years BW has been given only incidental attention as a subject of diplomatic discussion; for it seemed to have little bearing on the adjustments of power that were the main work of specialists in foreign affairs. However, BW does have something to do with efforts to reduce the barbarity of warfare. BW stands apart from all other devices in the actual threat that it poses to the health and life-expectancy of every human being whether or not he is politically involved in belligerent actions. In a word, the intentional release of an infectious particle, be it a virus or bacterium, from the confines of the laboratory or of medical practice must be condemned as an irresponsible threat against the whole human community.

The Black Death, the great bubonic plague that ravaged Europe in the mid-14th century is in fact a well documented historic example of just this process. The plague first entered Europe in 1346 via the sailors, rats, and fleas on the ships that returned to Genoa after having been expelled from Theodosia in the Crimea where the attacking Tartars had catapulted some of their corpses into the Genoese fortifications. This plague which reduced the population of Europe by at least one-third, would of course, almost surely have made its way West sooner or later, the nature of the disease being quite beyond the comprehension of the medical science of that era.

The Black Death in Europe was only one of many visitations of the plague suffered by Europe during the last 2000 years. We do not know why this one should have been so much more disastrous than many others. The progress of a disease in any given individual is subject to many factors of which only a few are well understood. A large epidemic, involving millions of people spread over time and space, is an immensely more complicated phenomenon about which it is very difficult to make accurate scientific predictions. This combination of very grave potential hazard with a high degree of unpredictability is a peculiar attribute of biological weaponry at its present stage of development. This has a great deal to do with the rational doctrine that so far has placed a relatively low value on its military utility.

The present situation thus might provide the most favourable opportunity for international action to regulate the further development and proliferation of BW. I am convinced we know enough about it to have legitimate concern about its future prospects. Until now no nation appears to have staked its security to any significant degree on BW armaments. I would therefore hope this provides a basis for accord. If we wait until BW has been developed into a reliable armament for use under a range of military doctrine, we must all fear that it could then be too late to disengage important powers from their commitment to it.

If I may return to the Black Death, the main barriers that may today keep bubonic plague from being a great threat in civilized countries are: (1) understanding of and the use of quarantine, (2) the suppression of rats and fleas by general urban hygiene, and (3) the use of modern therapy, especially antibiotics, to control the disease. Each one of these barriers could be breached by further technical developments if a substantial effort were to be applied during the next decade to making the plague bacillus into a weapon.

Other infectious agents might be even more adaptable. Some of man's deadliest enemies are viruses which, like yellow fever, are transmitted by mosquitos or other arthropods. These have the advantage, from a military standpoint, that they may not start a potentially retroactive epidemic in areas where the vector insect does not normally abound. It is already evident that such insect-borne viruses could be applied in the first instance by direct aerial dissemination, with little or no further spread from the first wave of infected targets. Recent reports of airborne or pneumonic rabies, a terrible disease, which as you know is normally spread by the bite of an infected dog or other animal, illustrate this possibility. There is then the danger that, if a large nucleus of people is attacked in this way, further evolution of the virus will occur to give rise to a new form of the disease that does spread from person to person, contrary to the calculations of the attacker. The Black Death itself underwent a similar evolution from the original bubonic flea-borne plague to outbreaks of the far more contagious pneumonic variety.

We have learned in recent years that viruses undergo constant evolution in their own natural history, not only by mutations within a given strain, but also by the natural cross-hybridization of viruses that superficially appear to be only remotely related to one another. Furthermore, many of us already carry viruses in our body cells of which we are unaware for years, and which may be harmless -- though they may eventually cause the formation of a tumor, or of brain degeneration, or of other diseases. At least in the laboratory, however, we can show that such latent viruses can still cross-breed with other viruses to give rise to many new forms.

My gravest concern is that similar scientific breakthroughs of a rather predictable kind will be made and their potential military significance exploited, so as to result in a transformation of current doctrine about "unreliable" biological weapons. We are all familiar with the process of mutual escalation in which the defensive efforts of one side inevitably contribute to further technical developments

on the other and vice versa. The mere existence of such a contest produces a mutual stimulation of effort; moreover, there is no practical system of counter-intelligence that will protect secret work for an indefinite period of time from becoming known to others. And the potential undoubtedly exists for the design and development of infective agents against which no credible defence is possible, through the genetic and chemical manipulation of these agents. It is thus clear to me that if we do not do something about this possibility, work will go forward and my fears will become realities.

Permit me, now, to ask a rhetorical question: Can we establish a world order that will, in effect, protect "you", as representatives of the global community, from the subversion of the scientific advances to which my own peers and myself have dedicated their careers.

I wish I could be sure that such a remark would always be received with an understanding of the ironic spirit with which it is uttered. I do not have to tell you of the worldwide attack on science, the flight from reason that has tempted so many young people and makes so many dilemmas for those of us in university life. This generational revolt has probably had its worst impact in countries which have already achieved a degree of affluence, but it is eroding the morale of the young even in those countries whose economic future most depends on their development of a high level of technical and scientific skill. What the youth see as the perversion of knowledge is, I believe, an important aspect of their repudiation of us. Among the undergraduates at my own university, there is no prospect more disheartening than the idea that even health research is subject to exploitation in the most inhumane direction imaginable.

For many years I have advocated that the control of biological warfare be given a special place in international and national initiatives for reasons I have mentioned. I am deeply gratified that President Nixon's announcement (last November 25) which disavowed offensive biological warfare development has made it possible for me to address these issues in terms fully consistent with the policy of the government of my own country.

As you know, soon after President Nixon's announcement it became apparent that the problem of toxins had been left ambiguous. "Toxins", as the term is understood by biologists, are chemical substances, usually (but not always) proteins of modest molecular size which are by-products of bacterial growth and which may play a lesser or greater role in the disease manifestations of a bacterial infection.

For present purposes we might think of a toxin as a chemical substance which would be unknown to science except for its association with microbial growth and one which has an extraordinarily high lethality per unit weight. Many toxins are nerve poisons, resembling the nerve gases in their effect on the body, but far more potent. For example, the lethal dose of botulinus toxin is about one millionth of a gram. This means that one could easily carry in a despatch case a quantity of toxin sufficient to wipe out the human population, although the image would imply that the human herd would line up for the slaughter. The very high potency of such toxins is certainly a factor in their military potential but may even be outweighed by other considerations, like the possibility of specific immunization of an aggressor force or population.

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Even after agreement to eliminate biological weapons, we will still remain very vulnerable to a form of biological warfare which is beyond the reach of any covenant that we can make. This is the warfare practised upon us by nature, the unremitting barrage of infection by old and by new agents that still constitute a very large part of the perils to normal and healthy life.

We have all had vexing, perhaps even tragic, personal experiences with virus infections. You will all recall the global epidemic of influenza that was first identified in Hong Kong about three years ago. This was not a particularly severe form of the virus and its eventual mortality was probably only in the tens of thousands. It is wrong, however, to believe that there is any assurance that the next epidemic of this kind will be as mild; and we have still developed only the most feeble and precarious protection against this threat whose impact is shared by all the nations, but against which very little common defence has been erected.

You will also recall having read from time to time about small outbreaks of mysterious new diseases like "Lassa fever" and the "Marbug virus". These were both extremely dangerous threats; and while much credit must be given to the diligence of the medical people who dealt with the outbreaks, a large element of pure luck was involved in localizing these incidents. We must expect that there are many additional viruses already indigenous to primate and human populations in primitive areas and to which the inhabitants of advanced countries are extremely vulnerable.

Yellow fever is a historically important disease which now belongs in the same category. It is now maintained on earth mainly through an animal reservoir of infection, in the monkeys in tropical jungles. Urban populations are now protected

from yellow fever by campaigns to abolish the fever-carrying species of mosquitos in South America and by the availability of excellent vaccines in advanced countries. Mosquito species very well capable of transmitting yellow fever are, however, abundant in South Asia and the accidental introduction of yellow fever, for example, into India would be a human tragedy of catastrophic dimensions. Specialists in epidemiology are quite puzzled that this accident has not already eventuated and we have no good explanation for this good fortune. I would not mention facts like these which might stimulate psychotic imaginations if they were not already well known. My purpose is not to suggest the vulnerability of the Asian continent to biological military attack but rather to point out immense gaps in the pattern of international co-operative defences that should be mounted but which have a relatively feeble standing in the present-day world. This is in no way a derogation of the splendid efforts of the World Health Organization which is centred here in Geneva but an indication of the limitations of its budget and a suggestion that much more needs to be done and could be done with resources that might be given over to biological work in the future.

Countries which are undergoing a transition in the development of their agriculture are vulnerable to analogous threats in biological warfare directed against crops as distinguished from human targets. The introduction of new crop varieties, that has had all of the human benefits attached to the expression "the green revolution", also means that the food supplies of vast territories are now committed to specialized strains of wheat, rice, and so forth. These are now newly vulnerable to destruction by plant pests of either natural or artificial origin. A potentially tragic outbreak of "coffee rust" is at this moment a serious threat to the agriculture and economy of Brazil.

The promulgation of an international agreement to control biological warfare in a negative sense should, therefore, be accompanied by steps urgently needed to build positive efforts at international co-operation, a kind of defensive biological research against natural enemies of the human species.

One of the best assurances that any country might have that the microbiological research of its neighbours was directed towards human purposes would be constantly expanding participation in international health programmes. Any country that publicly and avowedly subscribed to the total renunciation of secret BW research might conceivably be able to continue clandestine efforts without revealing their substantial content. It would, however, have great difficulty in maintaining such an

effort, at any substantial level or quality of operation, while still keeping its very existence secret. This applied especially to those among its own citizens who are specialists in health-oriented research and who are deeply involved in furthering health research activities within the framework of the international community. Therefore, besides the obvious direct health benefits of expanded international co-operation we would also be rewarded by a higher level of mutual assurance that every party was indeed living up to the spirit of its obligations under a BW convention.

In conclusion, let me say that some of the speculations I have mentioned are ones which all of us must fervently hope will never materialize. But it would seem to me both foolish and arrogant to assume that our good will alone, without concrete arrangements, will serve to forestall the further development, proliferation and possible eventual recourse to what surely is one of the most ghastly methods of warfare imaginable.

As a scientist whose research career has centred on the genetics of bacteria, I have a profound personal interest in efforts being made in this forum to minimize the risk that infectious disease will become a routine weapon in future conflicts, civil or international. You have heard reasons, that I believe are compelling, for promptly reaching a ban on the development, production, proliferation or use of biological weapons. I will be indebted to you for this opportunity if I can return to my laboratory with the hope of having made the most modest contribution to the fulfilment of the urgent task before you.

Good luck.